**Remarks**

Applicant has amended independent claim 29 to re-introduce the language "nicotinic acid", which was inadvertently left out of the request for amendment to claim 29 but included in claim 29 in Appendix A in the previous correspondence. Support for the amendment is found throughout the specification as filed and in claim 1 as originally presented. Applicant has also amended claim 30 to be dependent on claim 29, not claim 1. No new matter is added.

The Examiner stated that the Information Disclosure Statement filed January 4, 2005 is non-compliant under 37 C.F.R. §1.98(b)5 and MPEP 724.02. Applicant thoroughly reviewed these sections and was unable to determine what specifically was non-compliant. Applicant placed a call to the Patent Office and spoke with Supervisory Examiner Thurmond Page and Mr. Page instructed Applicant to state which claims the items on pages 1-3 of the Information Disclosure Statement pertain to. Applicant responds that these items do not necessarily apply to any claim. These items are allegations advanced by the Defendant in a patent lawsuit. In the interest of full disclosure, these items were provided to the Patent Office. As additional information, the parties have settled the lawsuit.

Entrance of the present amendment is respectfully requested and early passage of the above-referenced application for U.S. patent to issuance is earnestly solicited. Applicant has attached a copy of the previous response to the previous Office Action.

Should the Examiner have any questions or require additional information or clarification, Applicant requests that the Examiner contact the attorney of record at the number noted below.

Respectfully submitted,

Karen J. Messick, Esq.
Registration No. 42,256
Attorney for Applicants

KOS PHARMACEUTICALS, INC,
1 Cedar Brook Drive
Cranbury, NJ 08512
Tel: (609) 495-0568
Fax: (609) 495-0907

Date: 9/13/05

CERTIFICATION UNDER 37 C.F.R. §1.8

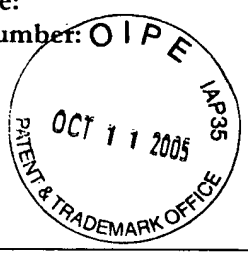
I hereby certify that this correspondence is being deposited with the United States Postal Service as First Class Mail in an envelope addressed to the Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450 on the date indicated below.

9/13/05
Date

Jared G. Silberhorn

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

| | |
|---|---|
| **Applicant:** | Eugenio Cefali, et al. |
| **Serial No.:** | 08/960,557 |
| **Filing Date:** | 31 October 1997 |
| **Docket Number:** | 50454-56103USCIP |
| **Title:** | METHODS FOR TREATING HYPERLIPIDEMIA WITH INTERMEDIATE RELEASE NICOTINIC ACID COMPOSITIONS HAVING UNIQUE BIOPHARMACEUTICAL CHARACTERISTICS |
| **Art Unit:** | 1615 |
| **Examiner:** | J.M. Spear |






Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

## TRANSMITTAL LETTER

Enclosed for filing in the above-identified patent application are the following documents:

1. Amendment under 37 CFR §1.312, as recommended by the Examiner;
2. Issue Fee payment and Issue Fee Transmittal letter;
3. Withdrawal of Small Entity Status; and
3. Return Postcard.

If there are any questions, please call the undersigned at the telephone number indicated below.

Respectfully submitted,

Kos Pharmaceuticals, Inc.

Karen J. Messick, Esq.
Attorney for Applicants
Reg. No. 46,256

Kos Pharmaceuticals, Inc.
1001 Brickell Bay Drive
25th Floor
Miami, Florida 33131
Tel.: (305) 523.3643
Fax.: (305) 377.4076

Date: 4/27/04

**CERTIFICATION UNDER 37 C.F.R., §1.10**

I hereby certify that the attached papers are being deposited with the United States Postal service as: "Express Mail Post Office to Addressee" Service under 37 C.F.R. §1.10 on 27 April 2004 and is addressed to Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

ER 593 968 481 US
Express Mail Label Number

Jared G. Silberhorn

PATENTS

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

| | |
|---|---|
| **In re Application of:** | CEFALI, EUGENIO |
| **Serial No.:** | 08/960,577 |
| **Filing Date:** | 13 October 1997 |
| **Docket Number:** | 50454-56103USCIP |
| **Title:** | METHODS FOR TREATING HYPERLIPIDEMIA WITH INTERMEDIATE RELEASE NICOTINIC ACID COMPOSITIONS HAVING UNIQUE BIOPHARMACEUTICAL CHARACTERISTICS |

COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, VA 22313-1450



## AMENDMENT AFTER ALLOWANCE UNDER 37 C.F.R. § 1.312

Sir:

A Notice of Allowance and Fee(s) Due was mailed January 27, 2004 for the above referenced patent application. After a final review by Applicant, it was discovered that an element of an independent claim was inadvertently claimed dependently. Applicant placed a call to the Examiner. After discussion, the Examiner recommended that Applicant file an Amendment after Allowance to the claims under 37 C.F.R. § 1.312.

Amendments to the Claims are reflected in the Listing of Claims, which begins on page 2 of this paper.

Remarks begin on page 3 of this paper.

(Remainder of page left intentionally blank.)

**Listing of Claims**

This listing of claims will replace all prior versions and listing of claims in this application. Pending and allowed claims are claims 29 through 61.



Please cancel claims 31, 37 and 43 without prejudice.

Please amend claim 29 as follows:

29. (Currently Amended) A method of treating cholesterol disorders with an intermediate release formulation without causing treatment limiting hepatotoxicity, elevations in uric acid, or glucose levels such that use of said formulation is discontinued comprising:

orally administering once per day an effective amount of said formulation for treating said disorder, said formulation having a dissolution curve similarity fit factor *F2* of at least about 79, and an *in vitro* dissolution profile, when measured in a type I dissolution apparatus (basket), according to U.S. Pharmacopiea XXII, in about 37°C in deionized water at about 100 rpm, s follows:

(a) less than about 15% of the nicotinic acid is released after about 1 hour in the apparatus;

(b) between about 15% and about 30% of the nicotinic acid is released after about 3 hours in the apparatus;

(c) between about 30% and about 45% of the nicotinic acid is released after about 6 hours in the apparatus

(d) between about 40% and about 60% of the nicotinic acid is released after about 9 hours in the apparatus;

(e) between about 50% and about 75% of the nicotinic acid is released after about 12 hours in the apparatus; and

(f) at least about 75% of the nicotinic is released after about 20 hours in the apparatus.

(Remainder of page left intentionally blank.)

COPY

Remarks

Applicant has amended independent claim 29 to include the phrase "a dissolution curve similarity fit factor *F2* of at least about 79" under 37 C.F.R. § 1.312, Amendment after Allowance, as recommended by the Examiner. This phrase is also the substance of dependent claims 31, 37 and 43. Thus, Applicant has canceled dependent claims 31, 37 and 43 without prejudice. Support for the amendment is found in the specification as filed pages 16-17 and in claim 1 as originally presented, copies of which are attached hereto. No new matter is added.

In Applicant's response of December 22, 2003, Applicant filed an amendment canceling all pending claims and submitting new claims as suggested by the Examiner in the Office Action of September 9, 2003. In the December 2003 amendment, Applicant inadvertently removed this phrase from an independent claim and moved it to dependent claims. The present amendment is needed because the phrase removed to currant claims 31, 37 and 47 is an element of the invention. This element provides a factor needed to properly analyze the results. After reviewing the application upon receiving the Notice of Allowance, the error was detected. The present amendment does not require further search or examination. The amended claims presented herewith are patentable as the only change is incorporating the phrase of independent claims 31, 37 and 47 to dependent claim 29. All of those claims were allowable in the Notice of Allowance mailed January 27, 2004.

Entrance of the present amendment is respectfully requested and early passage of the above-referenced application for U.S. patent to issuance is earnestly solicited. Applicant has included a clean copy of the pending claims in Appendix A. Should the Examiner have any questions or require additional information or clarification, Applicant requests that the Examiner contact the attorney of record at the number noted below.

Respectfully submitted,

Karen J. Messick, Esq.
Registration No. 42,256
Attorney for Applicants

KOS PHARMACEUTICALS, INC,
1001 Brickell Bay Drive
25th Floor
Miami, Florida 33131
Tel: (305) 523-3643
Fax: (305) 377-4076

Date: _____

CERTIFICATION UNDER 37 C.F.R. §1.10

I hereby certify that the attached papers are being deposited with the United States Postal service as: "Express Mail Post Office to Addressee" Service under 37 C.F.R. §1.10 on 27 April 2004 and is addressed to Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

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Express Mail Label Number Jared G. Silberhorn

29. A method of treating cholesterol disorders with an intermediate release nicotinic acid formulation without causing treatment limiting hepatotoxicity, elevations in uric acid, or glucose levels such that use of said formulation is discontinued comprising;

orally administering once per day an effective amount of said formulation for treating said disorder, said formulation having a dissolution curve similarity fit factor *F2* of at least bout 79, and an *in vitro* dissolution profile, when measured in a type I dissolution apparatus (basket), according to U.S. Pharmacopiea XXII, in about 37°C in deionized water at about 100 rpm, as follows:

(a) less than about 15% of the nicotinic acid is released after about 1 hour in the apparatus;

(b) between about 15% and about 30% of the nicotinic acid is released after about 3 hours in the apparatus;

(c) between about 30% and about 45% of the nicotinic acid is released after about 6 hours in the apparatus;

(d) between about 40% and about 60% of the nicotinic acid is released after about 9 hours in the apparatus;

(e) between about 50% and about 75% of the nicotinic acid is released after about 12 hours in the apparatus; and

(f) at least about 75% of the nicotinic acid is released after about 20 hours in the apparatus.

30. The method of claim 1, wherein approximately 100% of the nicotinic acid is released after about 20 hours in the apparatus.

31. (Cancelled)

32. The method of claim 29, wherein said formulation is a tablet.

33. The method of claim 32, wherein said tablet contains nicotinic acid in an amount selected from the group consisting of about 375mg, about 500mg and about 750mg.

34. The method of claim 29, wherein the once per day dose is administered during the evening or at night.

35. The method of 29, wherein the *in vitro* dissolution profile is as follows:

(a) between about 9.6% and about 13.8% of the nicotinic acid is released after about 1 hour in the apparatus;

(a) between about 21.2% and about 27.8% of the nicotinic acid is released after about 3 hours in the apparatus;

(b) between about 35.1% and about 44.2% of the nicotinic acid is released after about 6 hours in the apparatus;

(c) between about 45.6% and about 58.5% of the nicotinic acid is released after about 9 hours in the apparatus;

(d) between about 56.2% and about 72% of the nicotinic acid is released after about 12 hours in the apparatus; and

(e) at least about 75% of the nicotinic acid is released after about 20 hours in the apparatus.

36. The method of claim 35, wherein approximately 100% of the nicotinic acid is released after about 20 hours in the apparatus.

37. (Cancelled)

38. The method of claim 35, wherein said formulation is a tablet.

39. The method of claim 38, wherein said tablet contains nicotinic acid in an amount selected from the group consisting of about 375mg, about 500mg, and about 750mg.

40. The method of claim 35, wherein the once per day dose is administered during the evening or at night.

(Remainder of page left intentionally blank.)

41. The method of claim 29, wherein the *in vitro* dissolution profile is as follows:

(a) between about 9.8% and about 12.3% of the nicotinic acid is released after about 1 hour in the apparatus;

(b) between about 20.9% and about 26.7% of the nicotinic acid is released after about 3 hours in the apparatus;

(c) between about 35.3% and about 44.1% of the nicotinic acid is released after about 6 hours in the apparatus;

(d) between about 44.8% and about 58.7% of the nicotinic acid is released after about 9 hours in the apparatus;

(e) between about 59.5% and about 70.7% of the nicotinic acid is released after about 12 hours in the apparatus; and

(f) at least about 75% of the nicotinic acid is released after about 20 hours in the apparatus.

42. The method of claim 41, wherein approximately 100% of the nicotinic acid is released after about 20 hours in the apparatus.

43. (Cancelled)

44. The method of claim 41, wherein said formulation is a tablet.

45. The method of claim 44, wherein said tablet contains nicotinic acid in an amount selected from the group consisting of about 375mg, about 500mg, and about 750mg.

46. The method of claim 41, wherein the once per day dose is administered during the evening or at night.

(Remainder of page left intentionally blank.)

47. A method of treating cholesterol disorders with an intermediate release nicotinic acid formulation without causing treatment limiting hepatotoxicity, elevations in uric acid or glucose levels such that use of said formulation is discontinued, comprising;

orally administering once per day an effective amount of said formulation for treating said disorder, said formulation having a dissolution curve similarity fit factor *F2* of at least 44, and an *in vitro* dissolution profile, when measured in a type I dissolution apparatus (basket), according to U.S. Pharmacopiea XXII, in about 37°C in deionized water at about 100 rpm, as follows:

(a) less than about 15% of the nicotinic acid is released after about 1 hour in the apparatus;

(b) between about 15% and about 30% of the nicotinic acid is released after about 3 hours in the apparatus;

(c) between about 30% and about 45% of the nicotinic acid released after about 6 hours in the apparatus;

(d) between about 40% and about 60% of the nicotinic acid is released after about 9 hours in the apparatus;

(e) between about 50% and about 75% of the nicotinic acid released after about 12 hours in the apparatus; and

(f) at least about 75% of the nicotinic acid is released after about 20 hours in the apparatus.

48. The method of claim 47, wherein approximately 100% of the nicotinic acid is released after about 20 hours in the apparatus.

49. The method of claim 47, wherein said formulation is a tablet.

50. The method of claim 49, wherein said tablet contains nicotinic acid in an amount selected from the group consisting of about 375mg, about 500mg, about 750mg and about 1000mg.

51. The method of claim 47, wherein the once per day dose is administered during the evening or at night.

52. The method of claim 47, wherein the *in vitro* dissolution profile is as follows:

(a) between about 9.6% and about 13.8% of the nicotinic acid is released after about 1 hour in the apparatus;

(b) between about 21.2% and about 27.8% of the nicotinic acid is released after about 3 hours in the apparatus,

(c) between about 35.1% and about 44.2% of the nicotinic acid is released after about 6 hours in the apparatus,

(d) between about 45.6% and about 58.5% of the nicotinic acid is released after about 9 hours in the apparatus,

(e) between about 56.2% and about 72% of the nicotinic acid is released after about 12 hours in the apparatus, and

(f) at least about 75% of the nicotinic acid is released after about 20 hours in the apparatus.

53. The method of claim 52, wherein approximately 100% of the nicotinic acid is released after about 20 hours in the apparatus.

54. The method of claim 52, wherein said formulation is a tablet.

55. The method of claim 54, wherein said tablet contains nicotinic acid is an amount selected from the group consisting of about 375mg, about 500mg, and about 750mg.

56. The method of claim 52, wherein the once per day dose is administered during the evening or at night.

(Remainder of page left intentionally blank.)

57. The method of claim 47, wherein the *in vitro* dissolution profile is as follows:

(a) between about 9.8% and about 12.3% of the nicotinic acid is released after about 1 hour in the apparatus,

(b) between about 20.9% and about 26.7% of the nicotinic acid is released after about 3 hours in the apparatus,

(c) between about 35.3% and about 44.1% of the nicotinic acid is released after about 6 hours in the apparatus,

(d) between about 44.8% and about 58.7% of the nicotinic acid is released after about 9 hours in the apparatus,

(e) between about 59.5% and about 70.7% of the nicotinic acid is released after about 12 hours in the apparatus; and

(f) at least about 75% of the nicotinic acid is released after about 20 hours in the apparatus.

58. The method of claim 57, wherein approximately 100% of the nicotinic acid is released after about 20 hours in the apparatus.

59. The method of claim 57, wherein said formulation is a tablet.

60. The method of claim 59, wherein said tablet contains nicotinic acid in an amount selected from the group consisting of about 375mg, about 500mg, about 750mg and about 1000mg.

61. The method of claim 57, wherein the once per day dose is administered during the evening or at night.

Similarity between the test and the target dissolution curves within a tablet strength can be determined through the calculation of the fit factor $F_2$. See Moore JW, Flanner HH.: Mathematical comparison of dissolution profiles, Pharmaceutical Technology, 64-74 (June 1996), which is incorporated herein by reference in its entirety. In other words, the fit factor $F_2$ is calculated using the difference between the percent dissolved at each time point for each dissolution profile. If there is no difference between the percent dissolved at each time point, the fit factor $F_2$ equals 100. As the difference in percent dissolved increases, however, the fit factor $F_2$ value decreases. The fit factor $F_2$ is determined by the following equation:

$$F_2 = 50 \log \{[1 + 1/n \sum_{t=1}^{n} w_t (R_t - T_t)^2]^{-0.5} x\ 100\}$$

where $R_t$ is the dissolution value for the target profile at a time point $t$, $T_t$ is the dissolution value for the test profile at the same time point $t$, $n$ is the number of time points on the dissolution profile and $w_t$ is an optional weight factor. This equation is a logarithmic transformation of the sum of the mean square error between the test and target profile, resulting in a number between 0 and 100. The fit factor $F_2$ is 100 when two dissolution profiles are identical and decreases as the two profiles become more dissilimar. In other words, the smaller the fit factor $F_2$, the farther apart the products are from one another. The fit factor $F_2$ will be positive as long as the average difference between the two curves is 100 or less.

The following Table 6 depicts the recommended fit factor $F_2$ values for each of the Niaspan® tablet strengths. The recommended values are based on the range of fit factors $F_2$ between lots used in the New Drug Application (NDA), made more specific by the determination of bioequivalence to a target lot of Niaspan® tablets.

Having described my invention, I claim:

(1) A method of treating a lipidemic disorder with a nicotinic acid formulation suitable for oral administration once-a-day as a single dose without causing drug-induced hepatotoxicity in an individual to a level and without causing drug-induced elevations in uric acid or glucose or both to levels which would require use of the nicotinic acid formulation to be discontinued by the individual, comprising:

orally administering to the individual once-a-day as a single dose an effective amount of an intermediate release nicotinic acid formulation without causing drug-induced hepatotoxicity in the individual to a level and without causing drug-induced elevations in uric acid or glucose or both to levels which would require use of the intermediate nicotonic acid formulation by the individual to be discontinued, the intermediate release nicotinic acid formulation having

a dissolution curve similarity fit factor $F_2$ of at least about 79, and

an *in vitro* dissolution profile, when measured in a type I dissolution apparatus (basket), according to U.S. Pharmacopeia XXII, at about 37°C in deionized water at about 100 rpm, as follows

(a) less than about 15% of the nicotinic acid is released after about 1 hour in the apparatus,

(b) between about 15% and about 30% of the nicotinic acid is released after about 3 hours in the apparatus,

(c) between about 30% and about 45% of the nicotinic acid is released after about 6 hours in the apparatus,

(d) between about 40% and about 60% of the nicotinic acid is released after about 9 hours in the apparatus,

(e) between about 50% and about 75% of the nicotinic acid is released after about 12 hours in the apparatus, and

(f) at least about 75% is released after about 20 hours in the apparatus.

TABLE 6

| Criteria derived from: | 250 and 325 mg tablet strengths | 500mg tablet strength | 750mg tablet strength | 1000mg tablet strength |
|---|---|---|---|---|
| | | | | |
| Bioequivalence Studies | ≥79.0 | ≥79.0 | ≥79.0 | ≥44.0 |

The term "bioequivalence," as used herein, means the absence of a significant difference in the rate and extent to which the active ingredient or active moiety in pharmaceutical equivalents or pharmaceutical alternatives becomes available at the site of drug action when administered at the same molar dose under similar conditions in an appropriately designed study. See Code of Federal Regulations, Title 21, April 1, 1997 edition, Part 320.1, Definitions *(e) Bioequivalence*, page 195, which is incorporated by reference herein in its entirety.

Table 7 also depicts the fit factor $F_2$ for thirteen (13) of the sixteen (16) over-the-counter SR niacin products referenced in Tables 5A and 5B compared to the dissolution curve of Niaspan®. As can be seen from the fit factor $F_2$ data in Table 7, the thirteen (13) over-the-counter SR niacin products are not bioequivalent to Niaspan®, in view of the fact that the fit factor $F_2$ is less than 79 for all such products.

TABLE 7

| Brand | Niaspan® K4061A-1 500mg | GTRN 250 86A6014C 250mg | Nicobid MN0928 500mg | Goldline 12 12L51229 500mg | Goldline 87 87L51081 500mg | Goldline 89 89G5612C 500mg | Rugby M0 M070E 500mg | Rugby 5L 5L01707 500mg | Time Cap A051G 500mg | Major 5F00753 500mg | Upsher-Smith 16020 500mg | Geneva 4B124 500mg | Mason 501199 500mg | Endurance 11504 500mg | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| F2 | 79 | 54.3 | 39.4 | 60.6 | | 64.5 | 45.0 | 38.7 | 57.3 | 53.9 | 48.7 | 56.3 | 39.3 | 60.8 | 59.6 | |

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

| | |
|---|---|
| **In re Application of:** | CEFALI, EUGENIO |
| **Serial No.:** | 08/960,577 |
| **Filing Date:** | 13 October 1997 |
| **Docket Number:** | 50454-56103USCIP |
| **Title:** | METHODS FOR TREATING HYPERLIPIDEMIA WITH INTERMEDIATE RELEASE NICOTINIC ACID COMPOSITIONS HAVING UNIQUE BIOPHARMACEUTICAL CHARACTERISTICS |





**COMMISSIONER FOR PATENTS**
P.O. Box 1450
Alexandria, VA 22313-1450

## TRANSMITTAL OF ISSUE FEE

**MAIL STOP ISSUE FEE**
Commissioner For Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Dear Sir:

Enclosed herewith for filing in the above-identified application is an Issue Fee Transmittal Form PTOL-85 that was mailed on 27 January 2004. As the assignee no longer qualifies for Small Entity Status, a Withdrawal of Small Entity Status is also enclosed herewith. Therefore, please charge the requisite fee of $1330.00 to our Deposit Account 50-2543.

No additional fees are believed to be due in connection with this letter. However, please charge any additional costs or credit any overpayment to our Deposit Account No. 50-2543.

Respectfully submitted,

Kos Pharmaceuticals, Inc.

Karen J. Messick
Attorney for Applicants
Registration No. 46,256

Kos Pharmaceuticals, Inc.
1001 Brickell Bay Drive
25th Floor
Miami, FL 33131

Phone: 305.523.3643
Fax: 305.377.4076

Date: 4/27/04

**CERTIFICATION UNDER 37 C.F.R., §1.10**

I hereby certify that the attached papers are being deposited with the United States Postal service as: "Express Mail Post Office to Addressee" Service under 37 C.F.R. §1.10 on 27 April 2004 and is addressed to Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

ER 593 968 481 US
Express Mail Label Number

Jared G. Silberhorn

# PART B - FEE(S) TRANSMITTAL

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**Complete and send this form, together with applicable fee(s), to: Mail** Mail Stop ISSUE FEE
Commissioner for Patents
P.O. Box 1450
Alexandria, Virginia 22313-1450

**or Fax** (703) 746-4000

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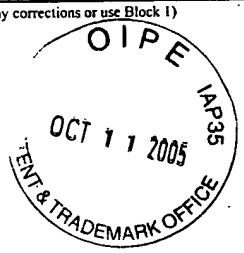
CURRENT CORRESPONDENCE ADDRESS (Note: Legibly mark-up with any corrections or use Block 1)

7590 01/27/2004

Karen J Messick ESQ
c/o KOS Pharmaceuticals Inc
1001 Brickell Bay Drive
25th Floor
Miami, FL 33131

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| |
|---|
| (Depositor's name) |
| (Signature) |
| (Date) |

| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|---|---|---|---|---|
| 08/960,557 | 10/31/1997 | EUGENIO A. CEFALI | 32892-00023 | 6174 |

TITLE OF INVENTION: METHODS FOR TREATING HYPERLIPIDEMIA WITH INTERMEDIATE RELEASE NICOTINIC ACID COMPOSITIONS HAVING UNIQUE BIOPHARMACEUTICAL CHARACTERISTICS

| APPLN. TYPE | SMALL ENTITY | ISSUE FEE | PUBLICATION FEE | TOTAL FEE(S) DUE | DATE DUE |
|---|---|---|---|---|---|
| nonprovisional | ~~YES~~ NO | ~~$665~~ $1330. - | $0 | $665 | 04/27/2004 |

| EXAMINER | ART UNIT | CLASS-SUBCLASS |
|---|---|---|
| SPEAR, JAMES M | 1615 | 424-468000 |

1. Change of correspondence address or indication of "Fee Address" (37 CFR 1.363).

☐ Change of correspondence address (or Change of Correspondence Address form PTO/SB/122) attached.

☐ "Fee Address" indication (or "Fee Address" Indication form PTO/SB/47; Rev 03-02 or more recent) attached. **Use of a Customer Number is required.**

2. For printing on the patent front page, list (1) the names of up to 3 registered patent attorneys or agents OR, alternatively, (2) the name of a single firm (having as a member a registered attorney or agent) and the names of up to 2 registered patent attorneys or agents. If no name is listed, no name will be printed.

1 KAREN J. MESSICK, ESQ.
2 _____
3 _____

3. ASSIGNEE NAME AND RESIDENCE DATA TO BE PRINTED ON THE PATENT (print or type)

PLEASE NOTE: Unless an assignee is identified below, no assignee data will appear on the patent. Inclusion of assignee data is only appropriate when an assignment has been previously submitted to the USPTO or is being submitted under separate cover. Completion of this form is NOT a substitute for filing an assignment.

(A) NAME OF ASSIGNEE: KOS PHARMACEUTICALS, INC

(B) RESIDENCE: (CITY and STATE OR COUNTRY): MIAMI, FLORIDA USA

Please check the appropriate assignee category or categories (will not be printed on the patent); ☐ individual ☑ corporation or other private group entity ☐ government

4a. The following fee(s) are enclosed:

☑ Issue Fee

☐ Publication Fee

☐ Advance Order - # of Copies _____

4b. Payment of Fee(s):

☐ A check in the amount of the fee(s) is enclosed.

☐ Payment by credit card. Form PTO-2038 is attached.

☑ The Director is hereby authorized by charge the required fee(s), or credit any overpayment, to Deposit Account Number 50-2543 (enclose an extra copy of this form).

Director for Patents is requested to apply the Issue Fee and Publication Fee (if any) or to re-apply any previously paid issue fee to the application identified above.

(Authorized Signature) _____ (Date) 4/27/04

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PATENTS

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

| | |
|---|---|
| **In re Application of:** | CEFALI, EUGENIO |
| **Serial No.:** | 08/960,577 |
| **Filing Date:** | 13 October 1997 |
| **Docket Number:** | 50454-56103USCIP |
| **Title:** | METHODS FOR TREATING HYPERLIPIDEMIA WITH INTERMEDIATE RELEASE NICOTINIC ACID COMPOSITIONS HAVING UNIQUE BIOPHARMACEUTICAL CHARACTERISTICS |

**COMMISSIONER FOR PATENTS**
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

## WITHDRAWAL OF SMALL ENTITY STATUS

Pursuant to 37 C.F.R. § 1.27(g)(2), Kos Pharmaceuticals Inc., the assignee in the above-identified application, hereby notifies the United States Patent and Trademark Office that assignee's status has changed and Small Entity status is no longer applicable.

Respectfully submitted,

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Date: 4/27/04

**CERTIFICATION UNDER 37 C.F.R., §1.10**

I hereby certify that the attached papers are being deposited with the United States Postal service as: "Express Mail Post Office to Addressee" Service under 37 C.F.R. §1.10 on 27 April 2004 and is addressed to Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

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